

# INTERNATIONAL SEARCH REPORT

Int'l Application No  
PCT/BE2004/000172

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61P25/24 A61K31/343 A61K31/4545 G01N33/48 A61K31/00  
A61P25/00 A61P25/28 A61P25/22 A61P25/16  
//(A61K31/4545, 31:343)

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K A61P G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, EMBASE, MEDLINE, WPI Data, PAJ, BIOSIS, CHEM ABS Data, SCISEARCH, PHARMAPROJECTS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 762 960 A (DODMAN NICHOLAS H) 9 June 1998 (1998-06-09) column 9, line 39 column 9, line 59 column 10, lines 20-26	1-81
X	VOLMAT R ET AL: "The treatment of depressions by Cledial. Evolution and clinical state and handwriting" PSYCHOLOGIE MEDICALE 1986 FRANCE, vol. 18, no. 10, 1986, pages 1615-1622, XP009028776 page 1620	1-81

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

9 May 2005

Date of mailing of the international search report

18/05/2005

Name and mailing address of the ISA

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/BE2004/000172

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>SQUELART P ET AL: "Pipamperone (Dipiperon), a useful sedative neuroleptic drug in troublesome chronic psychotic patients."            ACTA PSYCHIATRICA BELGICA. BELGIUM 1977 MAR-APR,            vol. 77, no. 2, March 1977 (1977-03),            pages 284-293, XP009028314            ISSN: 0300-8967            the whole document</p>	1-81
X	<p>DIEBOLD K. ET AL: "Are psychoactive-drug-induced changes in plasma lipid and lipoprotein levels of significance for clinical remission in psychiatric disorders?."            PHARMACOPSYCHIATRY, (1998) 31/2 (60-67)., 1998, XP009029360            table 2            page 61, column 1</p>	1-81
X	<p>KOCH H J ET AL: "Successful therapy of tardive dyskinesia in a 71-year-old woman with a combination of tetrabenazine, olanzapine and tiapride."            INTERNATIONAL JOURNAL OF CLINICAL PRACTICE. ENGLAND MAR 2003,            vol. 57, no. 2, March 2003 (2003-03),            pages 147-149, XP009030046            ISSN: 1368-5031            page 147, column 2, lines 1-3</p>	1-81
X	<p>WO 98/43646 A (BROEKKAMP CHRISTOPHORUS LOUIS ;PINDER ROGER MARTIN (NL); AKZO NOBE) 8 October 1998 (1998-10-08)            page 2, line 25; claims 3,8</p>	1-81
X	<p>PERUGI G ET AL: "EFFECTIVENESS OF ADJUNCTIVE GABAPENTIN IN RESISTANT BIPOLAR DISORDER: IS IT DUE TO ANXIOUS-ALCOHOL ABUSE COMORBIDITY?"            JOURNAL OF CLINICAL PSYCHOPHARMACOLOGY, WILLIAMS AND WILKINS, US,            vol. 22, no. 6, 2002, pages 584-591,            XP009029358            ISSN: 0271-0749            table 1</p>	1-81

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# INTERNATIONAL SEARCH REPORT

Int. Application No  
PCT/BE2004/000172

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ADLER L ET AL: "PRAXIS DER STATIONAEREN AKUTBEHANDLUNG VON MANIEN RETROSPEKTIVE VERGLEICHSUNTERSUCHUNG AN JE 100 PATIENTEN ZWEIER PSYCHIATRISCHER ZENTREN PRACTICE OF IN-PATIENT ACUTE TREATMENT OF MANIAS" FORTSCHRITTE DER NEUROLOGIE PSYCHIATRIE, STUTTGART, DE, vol. 62, no. 12, 1994, pages 479-488, XP009029389 ISSN: 0720-4299 page 483, column 2, last paragraph	1-81
X	ANSOMS C ET AL: "Sleep disorders in patients with severe mental depression: double-blind placebo-controlled evaluation of the value of pipamperone (Dipiperon)." ACTA PSYCHIATRICA SCANDINAVICA. FEB 1977, vol. 55, no. 2, February 1977 (1977-02), pages 116-122, XP009041169 ISSN: 0001-690X abstract	1-81
X	LEYSSEN J E ET AL: "RECEPTOR INTERACTIONS OF NEW ANTIPSYCHOTICS: RELATION TO PHARMACODYNAMIC AND CLINICAL EFFECTS" INTERNATIONAL JOURNAL OF PSYCHIATRY IN CLINICAL PRACTICE, MARTIN DUNITZ, LONDON, GB, vol. 2, no. 1, 1998, pages S03-S17, XP001009585 ISSN: 1365-1501 figure 2	1-81
X	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1996, SCHOTTE A ET AL: "Risperidone compared with new and reference antipsychotic drugs: In vitro and in vivo receptor binding" XP002290498 Database accession no. PREV199698829913 abstract & PSYCHOPHARMACOLOGY, vol. 124, no. 1-2, 1996, pages 57-73, ISSN: 0033-3158	1-81

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# INTERNATIONAL SEARCH REPORT

In **Patent** Application No  
PCT/BE2004/000172

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>VANHOENACKER P ET AL: "EFFICIENT EXPRESSION OF THE HUMAN DOPAMINE D4.2 RECEPTOR: POSITIVE INFLUENCE OF PIPAMPERONE ON EXPRESSION LEVELS" ABSTRACTS OF THE SOCIETY FOR NEUROSCIENCE, SOCIETY FOR NEUROSCIENCE, WASHINGTON, DC, US, vol. 26, no. 1/2, 2000, page 1, XP001181469 ISSN: 0190-5295 abstract</p>	1-81
X	<p>VIJVER VAN DE D A M C ET AL: "ANTIPSYCHOTICS AND PARKINSON'S DISEASE: ASSOCIATION WITH DISEASE AND DRUG CHOICE DURING THE FIRST 5 YEARS OF ANTIPARKINSONIAN DRUG TREATMENT" EUROPEAN JOURNAL OF CLINICAL PHARMACOLOGY, SPRINGER VERLAG, DE, vol. 58, no. 7, 2002, pages 157-161, XP009033980 ISSN: 0031-6970 abstract page 158, paragraph RESULTS; tables 1,2</p>	1-81
X	<p>ENGELBORGH S ET AL: "AMINO ACIDS AND BIOGENIC AMINES IN CEREBROSPINAL FLUID OF PATIENTS WITH PARKINSON'S DISEASE" NEUROCHEMICAL RESEARCH, PLENUM PRESS, NEW YORK, US, vol. 28, no. 8, August 2003 (2003-08), pages 1145-1150, XP009031514 ISSN: 0364-3190 abstract page 1147, column 1</p>	1-81
X	<p>DATABASE EMBASE 'Online! ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL; 1999, ETCHEPAREBORDA M C: "Neurocognitive and pharmacological approach to specific learning disorders" XP002311106 Database accession no. EMB-2000050033 abstract &amp; REVISTA DE NEUROLOGIA 1999 SPAIN, vol. 28, no. SUPPL. 2, 1999, pages S81-S93, ISSN: 0210-0010</p>	1-81
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## INTERNATIONAL SEARCH REPORT

In Application No  
PCT/BE2004/000172

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WIRZ-JUSTICE A ET AL: "HALOPERIDOL DISRUPTS, CLOZAPINE REINSTATES THE CIRCADIAN REST-ACTIVITY CYCLE IN A PATIENT WITH EARLY-ONSET ALZHEIMER DISEASE" ALZHEIMER DISEASE AND ASSOCIATED DISORDERS, RAVEN PRESS, NEW YORK, NY, US, vol. 14, no. 4, 2000, pages 212-215, XP009029353 ISSN: 0893-0341 table 1</p>	1-81
X	<p>FAHS H ET AL: "THYMOREGULATEURS DANS L'AGITATION ET LES TROUBLES DU COMPORTEMENT CHEZ LE SUJET DEMENT A PROPOS DE HUIT CAS ANTICONVULSIVANTS AND AGGRESSIVE BEHAVIORS IN ALZHEIMER'S DISEASE. EIGHT CASES REPORTS" ENCEPHALE, PARIS, FR, vol. 25, no. 2, 1999, pages 169-174, XP009039295 ISSN: 0013-7006 examples 1,3</p>	1-81
X	<p>GRÖZINGER M ET AL: "Melperone is an inhibitor of the CYP2D6 catalyzed O-demethylation of venlafaxine." PHARMACOPSYCHIATRY. GERMANY JAN 2003, vol. 36, no. 1, January 2003 (2003-01), pages 3-6, XP009029363 ISSN: 0176-3679 page 4, column 1</p>	1-81
X	<p>WERTH ESTHER ET AL: "Decline in long-term circadian rest-activity cycle organization in a patient with dementia." JOURNAL OF GERIATRIC PSYCHIATRY AND NEUROLOGY. 2002 SPRING, vol. 15, no. 1, April 2002 (2002-04), pages 55-59, XP009042127 ISSN: 0891-9887 table 1</p>	1-81
X	<p>DE 40 39 631 A (TROPONWERKE GMBH &amp; CO KG) 17 June 1992 (1992-06-17) claims 3,4,6</p>	1-81
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# INTERNATIONAL SEARCH REPORT

Int Application No  
PCT/BE2004/000172

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>STAHL STEPHEN M ET AL: "Examination of nighttime sleep-related problems during double-blind, placebo-controlled trials of galantamine in patients with Alzheimer's disease."</p> <p>CURRENT MEDICAL RESEARCH AND OPINION. APR 2004, vol. 20, no. 4, April 2004 (2004-04), pages 517-524, XP009041652 ISSN: 0300-7995 abstract table 2</p>	1-81
A	<p>-----</p> <p>DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1995, MELTZER HERBERT Y ET AL: "Plasma clozapine levels and the treatment of L-DOPA-induced psychosis in Parkinson's disease. A high potency effect of clozapine" XP002290499 Database accession no. PREV199598192811 abstract &amp; NEUROPSYCHOPHARMACOLOGY, vol. 12, no. 1, 1995, pages 39-45, ISSN: 0893-133X</p>	1-81
A	<p>-----</p> <p>MUENCHAU A ET AL: "PHARMACOLOGICAL TREATMENT OF PARKINSON'S DISEASE" POSTGRADUATE MEDICAL JOURNAL, MCMILLAN PRESS, BASINGSTOKE, GB, vol. 76, no. 900, October 2000 (2000-10), pages 602-610, XP009034316 ISSN: 0032-5473 the whole document</p>	1-81
A	<p>-----</p> <p>FALTRACO F ET AL: "AKTUELLE THERAPIEMOEGLICHKEITEN DER ALZHEIMER DEMENZ CURRENT THERAPEUTICAL STRATEGIES IN DEMENTIA" NEUROLOGIE UND REHABILITATION, BONN, DE, vol. 9, no. 1, 2003, pages 15-22, XP009041267 ISSN: 0947-2177 the whole document</p>	1-81
A	<p>-----</p> <p>WO 02/051833 A (H. LUNDBECK A/S; KEHLER, JAN; BANG-ANDERSEN, BENNY) 4 July 2002 (2002-07-04) page 4, lines 28-30 page 16, lines 15-21</p> <p>-----</p>	1-81

Continuation of Box II.2

Claims Nos.: 79

Present claim 79 is a "reach-through claim" which lacks clarity and support within the meaning of Art. 6 PCT and disclosure within the meaning of Art. 5 PCT.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/BE2004/000172

## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 79  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.



# INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No  
PCT/BE2004/000172

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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